REMARKS

Claims 23-26 and new claims 27-29 are pending.

Amendments

Claims 23 and 24 have been amended to delete the "." before the recitation of "p53-gln^{248}." This amendment is merely clerical in nature and does not narrow the scope of the claims. Claim 23 has also been amended to recite "cancer, arterial restenosis, and undesirable immune response accompanying rejection of a transplant or an autoimmune disease" in place of "cancer, and arterial restenosis, undesirable immune response accompanying rejection of a transplant and an autoimmune disease." This amendment also merely corrects formal matters and does not narrow the scope of claim 23.

New claim 27 is directed to a method of activating DNA binding activity of p53. The specification supports such methods at page 7, lines 10-12: "According to this invention, peptides are provided that activate the DNA binding activity of the wild-type form of the p53 tumor suppressor, as well as of certain tumor-derived p53 mutants." The method comprises a step of "administering" that is similar to and supported by the step of "administering" recited in claims 23 and 24. New claims 28 and 29 are similar to and supported by claims 25 and 26.

None of these amendments introduce new matter.

The Rejection of Claims 23-26 Under 35 U.S.C. § 112, First Paragraph

Claims 23-26 are rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. Applicants respectfully traverse.

The enablement requirement 35 U.S.C. § 112, first paragraph, states that a patent specification must teach a person skilled in the relevant art how to make and use the claimed invention. The need for some experimentation or routine screening does not mandate a finding of non-enablement. *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (Bd. App. 1982). A therapeutic invention need not be refined to the point where clinical efficacy in patients can be demonstrated

in order to be patentable. *In re Brana*, 51 F3d 1560 (Fed. Cir. 1995). The specification satisfies the enablement requirement.

The Office Action, however, asserts that the claims are not enabled because it is questionable whether the specification adequately discloses whether the claimed methods can be successfully used in the claimed methods. Specifically, the Office Action asserts:

> [T]he claims are directed to in vivo treatments and such treatments, in and of themselves, are unpredictable because pharmacokinetic factors such as the stability of the peptides in the body, half-life, absorption efficiency, binding affinity for target cells, biotransformation, and the rate of clearance from the body are important consideration for the efficacy of the claimed subject matter and yet have not been considered.

Paper 5, page 3, lines 9-13. Contrary to the assertions in the Office Action, it is not necessary for the specification to disclose clinical data proving the efficacy of the claimed methods to satisfy the enablement requirement.

Nevertheless, the specification supports the enablement of the claimed methods. The specification discloses that the administered peptides (peptides having at least four sequential amino acids from a negative regulatory region which maps to residues 361-383 of p53) activate DNA binding of wild-type p53 and p53 mutant polypeptides as recited in the claims. Example 5 describes an assay in which the p53 peptides administered in the claimed methods are added to *in vitro* translated p53 or select p53 mutants. Double-stranded oligonucleotides encoding p53 DNA binding sites were also present in the assay mixture to detect DNA binding activity of the p53 or mutant p53 molecules in the presence or the absence of the recited p53 peptides. Example 5 found that the peptides activate DNA binding of the p53 proteins: "[T]he peptides of this invention activate DNA binding and select p53 mutants." Page 28, lines 24-25; See also Table 3, page 29. Thus, the recited p53 peptides activate DNA binding, their claimed activity in the methods.

Furthermore, the specification discloses modifications of the recited p53 peptides that will increase their effectiveness *in vivo*, demonstrating that applicants have contemplated factors

that must be considered to perform the treatment methods. The specification discloses,

> While the peptides described above are effective in activating DNA binding of wild-type p53 *in vitro*, their effectiveness *in vivo* might be compromised by the presence of proteases. . . . Based on these considerations, it is advantageous to utilize modified versions of the peptides described above. The modified peptides retain the structural characteristics of the original L-amino acid peptides that confer biological activity with regard to p53, but because of the modification, they are not readily susceptible to cleavage by proteases and/ or exopeptidases.

Page 9, lines 20-30. The specification then describes modifications of the recited p53 peptide that increase its stability *in vivo* such as including an N-terminal D-amino acid (page 10, lines 8-14), including a C-terminal D-amino acid (page 10, lines 15-21), cyclizing the peptide (page 10, lines 22-27), substituting unnatural amino acids (page 10, line 28 to page 11, line 8), and adding N-terminal or C-terminal chemical groups (page 11, lines 9-21). These modifications of the recited p53 peptides could readily be made by one of skill in the art by routine methods. The disclosure in the specification that the recited p53 peptides activate p53 proteins coupled with the disclosure in the specification of stabilizing modifications of the recited p53 peptides enable one of skill in the art to practice the claimed methods.

New claims 27-29 should not subject to this rejection. These claims are directed to methods of activating DNA binding activity of a p53 polypeptide. These methods are clearly enabled by Example 5 in the specification, described above. "The enablement requirement is met if the description enables any mode of making and using the claimed invention." *Engel Industries, Inc. v. Lockformer Company*, 946 F.2d 1528, 1533 (Fed. Cir. 1991).

Accordingly, Applicants respectfully request reconsideration, withdrawal of the rejection of claims 23-26, and request a written indication of the allowance of these claims together with the allowance of new claims 27-29.

Respectfully submitted,

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